Agreement was reached that the amendments set forth in the present paper would obviate all outstanding rejections, including all rejections under 35 U.S.C. § 112. However, the Examiners stated that such amendments would obligate a new search and would therefore not be entered absent the filing of a request for continued examination.

Specification support for claim amendments

Support for the term "nonhairpin" may be found throughout the specification and drawings, and particularly as follows: page 9, lines 23 - 28; page 10, lines 19 - 23; page 2, lines 12 - 17; page 6, lines 2 - 4; page 6, lines 14 - 17; page 6, line 30 - page 7, line 6; page 7, lines 7 - 11; page 7, lines 23 - 27; page 9, lines 4 - 9; page 10, lines 27 - 29; page 16A, lines 8 - 11; page 19, lines 3 - 7; page 22, lines 10 - 12; page 22, lines 18 - 24; page 22, lines 25 - 27; page 32, lines 4 - 7; page 33, lines 8 - 10.

Support for the language "wherein said cultured or selectively enriched cells are not human embryonic stem cells" may be found particularly at page 6, lines 17 - 18; page 7, lines 11 - 17; and page 22, lines 2 - 3. *See also* MPEP § 2173.05(i) and *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977).

Comments

Applicants respectfully traverse all rejections, and reserve the right to prosecute claims identical to those

pending prior to the instant amendment in one or more continuation or divisional applications. Applicants explicitly reserve the right to prosecute claims reading on modification of human ES cells in one or more continuation or divisional applications.

Applicants respectfully state that the amendments presented herein are motivated solely by business exigencies, and with respect to the exclusion of human embryonic stem cells, additionally by the recognition of political imperatives, and do not by such amendments admit to or acquiesce in the rejections.

Respectfully submitted,

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Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. § 1.121(c)(ii)

25 (twice amended). A method of targeted sequence alteration of a nucleic acid **present within selectively enriched cells, cells in culture, or cell-free extracts**, comprising:

combining the targeted nucleic acid[,] in the presence of cellular repair proteins **[present within selectively enriched cells, cells in culture, or cell-free extracts,]** with a single-stranded **nonhairpin** oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a**[n]** **[internally unduplexed]** domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the nucleic acid target, but for one or more mismatches as between the sequences of said **[internally unduplexed]** deoxyribonucleotide domain and its complement on **[said]** **the** target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini[,] **[and]** ;

wherein said oligonucleotide has at least one terminal modification selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages, **and**

wherein said cultured or selectively enriched cells are not human embryonic stem cells.

75 (twice amended). A method of targeted sequence alteration of a nucleic acid **present within selectively enriched cells, cells in culture, or cell-free extracts**, comprising:

combining the targeted nucleic acid[,] in the presence of cellular repair proteins **[present within selectively enriched cells, cells in culture, or cell-free extracts,]** with a single-stranded **nonhairpin** oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a **[n] [internally unduplexed]** domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the nucleic acid target, but for one or more mismatches as between the sequences of said **[internally unduplexed]** deoxyribonucleotide domain and its complement on **[said] the** target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini[,] **[and]** ;

wherein said oligonucleotide has at least one terminal modification, **[and] said oligonucleotide** includes the sequence of any one of SEQ ID NOs: 1 - 4340[.], **and said cultured or selectively enriched cells are not human embryonic stem cells.**